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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/464,303	12/15/1999	GREGORY L. STAHL	B0801/7156	7348

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EXAMINER

VANDERVEGT, FRANCOIS P

ART UNIT	PAPER NUMBER
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1644

DATE MAILED: 10/11/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/464,303	Applicant(s) STAHL ET AL.	
	Examiner F. Pierre VanderVegt	Art Unit 1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 06 September 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 63-85 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 80-82 is/are allowed.
- 6) ☒ Claim(s) 63-68, 72-79 and 83-85 is/are rejected.
- 7) ☒ Claim(s) 69-71 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

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DETAILED ACTION

The Examiner in charge of your application in the USPTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to F. Pierre VanderVegt, Ph.D. in Art Unit 1644.

Claims 1-62 have been canceled.

New claims 63-85 have been added and are the subject of examination in the present Office Action.

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on September 3, 2005 has been entered.
2. Applicant's arguments filed September 6, 2005 have been fully considered but are not persuasive. In view of Applicant's request for continued examination under 37 CFR 1.114, the following grounds of rejection have been maintained in a modified form. This Office Action is made NON-FINAL.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 63-68, 72-79 and 83-85 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

The claims are broadly drawn to an antibody or fragment thereof that binds to human MBL wherein the antibody comprises a CDR3 region of one of 3 deposited monoclonal antibodies. Claim 75 recites the further limitation that the claimed antibody also comprises a CDR2 region from one of the monoclonal antibodies, but is silent about the presence of a CDR1 region. Claim 77 recites the further

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limitation that the claimed antibody also comprises a CDR1 region from one of the monoclonal antibodies, but is silent about the presence of a CDR2 region. The claims do not require that the CDR regions are obtained from the same antibody or from the same chain of the antibody. The specification does not disclose the amino acid sequence of any of the monoclonal antibodies or of any portion of the monoclonal antibodies.

The CDR3 region of an immunoglobulin molecule is only about 8-9 amino acid residues in length. However, based upon a 9 amino acid segment (which has not been sequenced), the instant claims broadly recite any antibody, or antigen-binding fragment thereof, that binds to mannose binding lectin. The specification does not teach the individual isolation of the CDR1, CDR 2 or CDR3 region of the heavy or light chain of any of the three disclosed deposited monoclonal antibodies. Furthermore the specification does not teach that any of the six CDR regions from any of the three disclosed deposited antibodies are capable of binding mannose-binding lectin on their own. The specification discloses only the ability of the monoclonal antibodies 3F8, 2A9 and hMBL1.2 to bind mannose-binding lectin.

Vas-Cath Inc. v. Mahurkar ((CAFC, 1991) 19 USPQ2d 1111), clearly states that "Applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See *Vas-Cath* at page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 USC 112 is severable from its enablement provision (see *Vas-Cath* at page 1115).

Applicant's deposit demonstrates only possession of a single monoclonal antibody possessing the CDRs of monoclonal antibody 3F8, and that is the monoclonal antibody 3F8 produced by the hybridoma cell line deposited under ATCC Accession No. HB-12621. Applicant's deposit demonstrates only possession of a single monoclonal antibody possessing the CDRs of monoclonal antibody hMBL1.2, and that is the monoclonal antibody hMBL1.2 produced by the hybridoma cell line deposited under ATCC Accession No. HB-12619. Applicant's deposit demonstrates only possession of a single monoclonal antibody possessing the CDRs of monoclonal antibody 2A9, and that is the monoclonal antibody 2A9 produced by the hybridoma cell line deposited under ATCC Accession No. HB-12620.

Therefore, despite Applicant's contention that possession of the deposited monoclonal antibodies as a whole molecule entitles Applicant to consideration as being in possession of the individual CDR regions contained in those antibodies, a lack of a description of the actual structure of the individual CDR regions and a lack of a description of the actual binding properties of the individual CDR regions

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demonstrates instead that Applicant was not in possession of those individual CDRs as mannose binding ligands as part of any other antibody or antigen binding fragment thereof. Applicant has demonstrated only the possession of the deposited monoclonal antibodies and antigen binding fragments thereof.

Applicant's citation in the response of the work of others that CDR3 regions of some antibodies are able to bind antigen as an individual peptide (without CDR1 or CDR2 involvement) is not pertinent to the instant case. The cited references show only the work of others demonstrating specifically that the CDR3 regions of their disclosed antibodies are able to bind antigen. The references do not, however, speak to the ability of the CDR3 regions of 3F8, 2A9 and hMBL1.2 to specifically bind mannose-binding ligand and neither does the instant specification. Adequate written description requires more than a mere statement that it is part of the invention. See *Fiers v. Revel*, ((CAFC, 1993) 25 USPQ 2d 1601) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, ((CAFC, 1991) 18 USPQ2d 1016).

4. Claims 63-68, 72-79 and 83-85 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an antibody produced by the hybridoma cell lines 2A9, 3F8 and hMBL1.2 and antigen-binding fragments thereof does not reasonably provide enablement for the broader recitation of any antibody or antigen binding fragment thereof comprising an MBL CDR3 region extracted from 2A9, 3F8 or hMBL1.2. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required are summarized in *Ex parte Forman*, 230 USPQ 546 (BPAI 1986). They include the nature of the invention, the state of the prior art, the relative skill of those in the art, the amount of direction or guidance disclosed in the specification, the presence or absence of working examples, the predictability or unpredictability of the art, the breadth of the claims, and the quantity of experimentation which would be required in order to practice the invention as claimed.

The claims are broadly drawn to an antibody or fragment thereof that binds to human MBL wherein the antibody comprises a CDR3 region of one of 3 deposited monoclonal antibodies. Claim 75 recites the further limitation that the claimed antibody also comprises a CDR2 region from one of the monoclonal antibodies, but is silent about the presence of a CDR1 region. Claim 77 recites the further limitation that the claimed antibody also comprises a CDR1 region from one of the monoclonal antibodies, but is silent about the presence of a CDR2 region. The claims do not require that the CDR regions are obtained from the same antibody or from the same chain of the antibody. The specification

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does not disclose the amino acid sequence of any of the monoclonal antibodies or of any portion of the monoclonal antibodies.

The CDR3 region of an immunoglobulin molecule is only about 8-9 amino acid residues in length. However, based upon a 9 amino acid segment (which has not been sequenced), the instant claims broadly recite any antibody, or antigen-binding fragment thereof, that binds to mannose binding lectin. The specification does not teach the individual isolation of the CDR1, CDR 2 or CDR3 region of the heavy or light chain of any of the three disclosed deposited monoclonal antibodies. Furthermore the specification does not teach that any of the six CDR regions from any of the three disclosed deposited antibodies are capable of binding mannose-binding lectin on their own. The specification discloses only the ability of the monoclonal antibodies 3F8, 2A9 and hMBL1.2 to bind mannose-binding lectin.

In order to engineer other antibodies comprising the CDR regions of one of the instantly disclosed deposited antibodies there is a requirement for sequence information for the CDR regions themselves. Sequence information is also needed for the framework regions flanking the CDRs in order to graft the CDR into an immunoglobulin molecule and to properly orient the CDR for antigen binding. However, the specification fails to provide any sequence information whatsoever regarding the CDR and framework regions of the heavy or light chains of monoclonal antibodies 3F8, 2A9 and hMBL1.2.

Janeway et al. (Immunobiology 4th Edition [1999] page87; of record) teaches that the CDR1, CDR2 and CDR3 regions of the heavy and light chains determine antigen specificity of an antibody. Applicant has argued, in regard to the Janeway reference, that CDR1 and CDR2 "might further contribute partially to binding," in asserting that Janeway stresses the importance of CDR3 to binding. In fact, Janeway treats CDR1, CDR2, and CDR3 equally and does not emphasize any one over the others. Further, Janeway clearly shows that not only are all three CDRs important, but the intervening framework sequences contribute significantly to the 3-dimensional relationship of CDR1, CDR2, and CDR3 to one another, orienting the CDRs properly for forming the binding site. Applicant's further contention that peptides comprising the CDR3, in the form of F(ab) and F(ab')₂ fragments, have been shown bind MBL is not convincing to support the broad recitation of the claims, as applicant is reminded that F(ab) and F(ab')₂ fragments also comprise CDR1 and CDR2 regions and comprise both the heavy chain variable region and the light chain variable region, meaning that the Ab fragments have CDR1, CDR2, and CDR3 contributions from both chains.

Applicant continues to assert that articles by Laune, Monnet, Taub and Igarashi (citations on page 9 of response filed April 24, 2004) support the argument that peptides comprising the CRD3 would be able to bind MBL. However, each of the references teaches that CDR-containing fragments of the

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antibodies from which they are derived are capable of binding to the target antigen. The cited references show only the work of others demonstrating specifically that the CDR3 regions of their disclosed antibodies are able to bind antigen. The references do not, however, speak to the ability of the CDR3 regions of 3F8, 2A9 and hMBL1.2 to specifically bind mannose-binding ligand and neither does the instant specification.

In view of the limited working examples, the unpredictability of the art, the lack of sufficient guidance in the specification and the breadth of the claims, it would take undue trials and errors to practice the claimed invention and the statute does not sanction this.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 63-68, 72-79 and 83-85 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 63 is ambiguous and unclear in the recitation of "comprising: a CDR3 of a monoclonal antibody" in lines 2-3. Dependent claim 68, which is supposed to be further limiting than base claim 63, recites "wherein the antibody or fragment thereof is a monoclonal antibody." Does this claim imply, therefore, that base claim 63 also encompasses polyclonal antibodies? However, the recitation in claim 63 of a particular CDR3 implies that the antibody would be inherently monoclonal or engineered, in which case claim 68 would fail to further limit the base claim. Additionally, reading claim 63 upon an antibody in a polyclonal preparation would raise enablement issues regarding the ability to determine the CDR3 sequence of a particular antibody in the preparation. Clarification is required.

Allowable Subject Matter

6. Claims 80-82 are allowed.

7. Claims 69-71 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

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Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to F. Pierre VanderVegt whose telephone number is (571) 272-0852. The examiner can normally be reached on M-Th 6:30-4:00 and Alternate Fridays 6:30-3:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

F. Pierre VanderVegt, Ph.D.
Patent Examiner
September 27, 2005

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David A Saunders
DAVID SAUNDERS
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